Please add new claim 24.

24. (New) A pharmaceutical formulation comprising a pharmaceutically acceptable excipient and a anti-bacterially or anti-fungally effective amount of a compound of any one of claims 1, 2, or 4 - 17.

REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining in this application be allowed.

Amendments

Claims 3 and 18 have been canceled without prejudice, solely for the purpose of expediting prosecution. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent applications.

Claim 1 has been amended to recite that X^2 is a fused bicyclic or tricyclic heteroaryl group and to more clearly define R^3. Support for fused bicyclic or tricyclic heteroaryl groups can be found, for example, on page 6 line 35 - 37 of Applicants' specification.

Claim 5 has been amended to include a Markush grouping of fused bicyclic or tricyclic heteroaryl groups from which X^2 can be chosen and to reflect proper dependency.

Claim 6 has been amended to correct a typographical error and to more clearly define R^6.

Claim 9 has been amended to correct a typographical error.

Claim 24 is newly presented and is supported by the specification at, for example, page 3, lines 24 - 27.

No new matter has been added. Entry of these amendments is requested.

Upon entry of the above amendments, Claims 1, 2, and 4 - 17 remain in this application.

Rejection Under 35 U.S.C. §103(a)

Claims 1-18 stand rejected under 35 U.S.C. §103(a) over Lown *et al.*, US Patent No 5,616,606 ("Lown"). For the following reasons, this rejection is traversed.

Initially, Applicants note that the test for non-obviousness articulated by the Court of Appeals for the Federal Circuit in *In re Vaeck* requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition; and (2) whether the prior art would also have provide a reasonable expectation of success to such a skilled artisan. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

This requirement goes to the question of motivation, and refers to a well established holding from earlier case law that there must be some logical reason at the time of the invention for combining the references along the lines of the invention; otherwise the use of the teachings as evidence of non-obviousness will entail prohibited hindsight. *Ex parte Stauber and Eberle*, 208 U.S.P.Q. 945, 946 (Bd. App. 1980).

The claimed invention is directed to compounds and pharmaceutical compositions. In the claimed invention, however, the X^2 substituent is a fused bicyclic or tricyclic heteroaryl group and furthermore, the claimed compounds are trimeric -- containing three aryl or heteroaryl groups including the X^2 substituent noted above.

Contrarily, Lown specifically recites that, R^1 is a derivative of a dicarboxylic acid (or is a residue of a carbonic acid (see Col 5, Lines 1 - 5)) that is 1) a derivative of a 5 or six member aromatic ring, wherein one of the ring carbons may optionally be a nitrogen group, (see Col. 5, lines 6 -12, of Lown), 2) a derivative of an unsaturated alkane, (see Col 5, Lines 13-18), 4) a derivative of a cycloalkane, optionally fused to one or more additional 3 to 7 C membered rings (see Col 5, Lines 19-27) or 5) a derivative of an

unsaturated cycloalkane (see Col 5, Lines 28-32). At best, Lown's group R^1, which corresponds to (O)C-X^2-C(O) of Applicants' compounds of Formula I, can be a single ring nitrogen-containing heteroaryl group. Lown, however, does not disclose fused bicyclic or tricyclic heteroaryl groups as found in the now claimed invention. Accordingly, Applicants submit that Lown fails to establish a *prima facie* case of obviousness.

The Office Action alleges that the structures depicted by Lown are structurally similar to those of the claimed invention because they contain a similar structural core. Applicants take issue with any such an allegation. In this regard, a mere similarity in structure can not automatically be equated with *prima facie* obviousness. *In re Coes*, 81 U.S.P.Q. 369 (CCPA 1949); *In re Langer*, 175 U.S.P.Q. 169 (CCPA 1972). There must be some motivation provided to make the requisite compound. *In re Lalu*, 223 U.S.P.Q. 1257 (Fed. Cir. 1984). In addition the requisite motivation to prepare the compounds of the claimed invention must come from the prior art and not Applicants' disclosure. No such motivation is present in Lown.

Specifically, the claimed invention requires a fused bicyclic or tricyclic heteroaryl group which is neither disclosed nor suggested by Lown. Moreover, the Office Action fails to recite why one skilled in the art would be motivated by Lown to construe that the single ring nitrogen-containing heteroaryl groups disclosed therein would have the same structural core as the fused bicyclic or tricyclic heteroaryl group of the now claimed invention.

In addition to the above, Applicants maintain that, even if one were to assume arguendo that the claimed fused bicyclic or tricyclic heteroaryl groups are similar to those of Lown, there is simply no expectation provided in the art that the compounds of this invention will possess anti-fungal and/or antibacterial properties. While the Office Action asserts that antibacterial and antiretroviral activity are interchangeable, this is an unsubstantiated assertion that one of ordinary skill in the art would not consider to be an

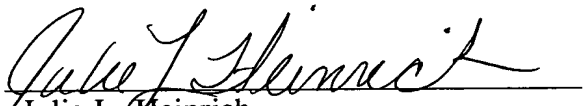
accurate reflection of what is generally known about the modes of action of antibacterial and antiretroviral drugs.

Finally, despite the absence of motivation to do so, even if one were to replace the single ring nitrogen-containing heteroaryl groups in Lown's compounds with fused bicyclic or tricyclic heteroaryl groups, absent evidence to contrary, there would have been no reasonable expectation that these compounds would have the anti-fungal and/or antibacterial properties that have been demonstrated in the present application.

Applicants submit that this application is now in condition for allowance. A Notice to that effect is earnestly requested.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: 
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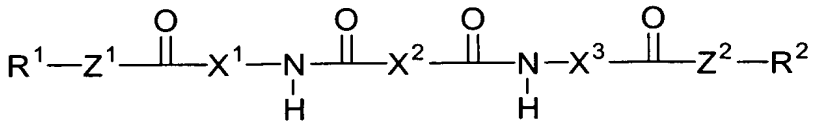
Date: September 9, 2002

Marked Up Copy of the Claims

1. (amended) A compound of Formula (I):



(I)

wherein:

Z^1 and Z^2 are independently -NR^3- **[(wherein R^3 is hydrogen or alkyl)]** or -O-;

R^1 and R^2 are independently substituted alkyl, substituted aryl, heteroaryl, or substituted heteroaryl provided that at least one of R^1 and R^2 is a group that can form a pharmaceutically acceptable acid addition salt;

R^3 is hydrogen, alkyl or R^3 and R^1 or R^2 together with the atoms to which they are attached form a heterocyclic ring;

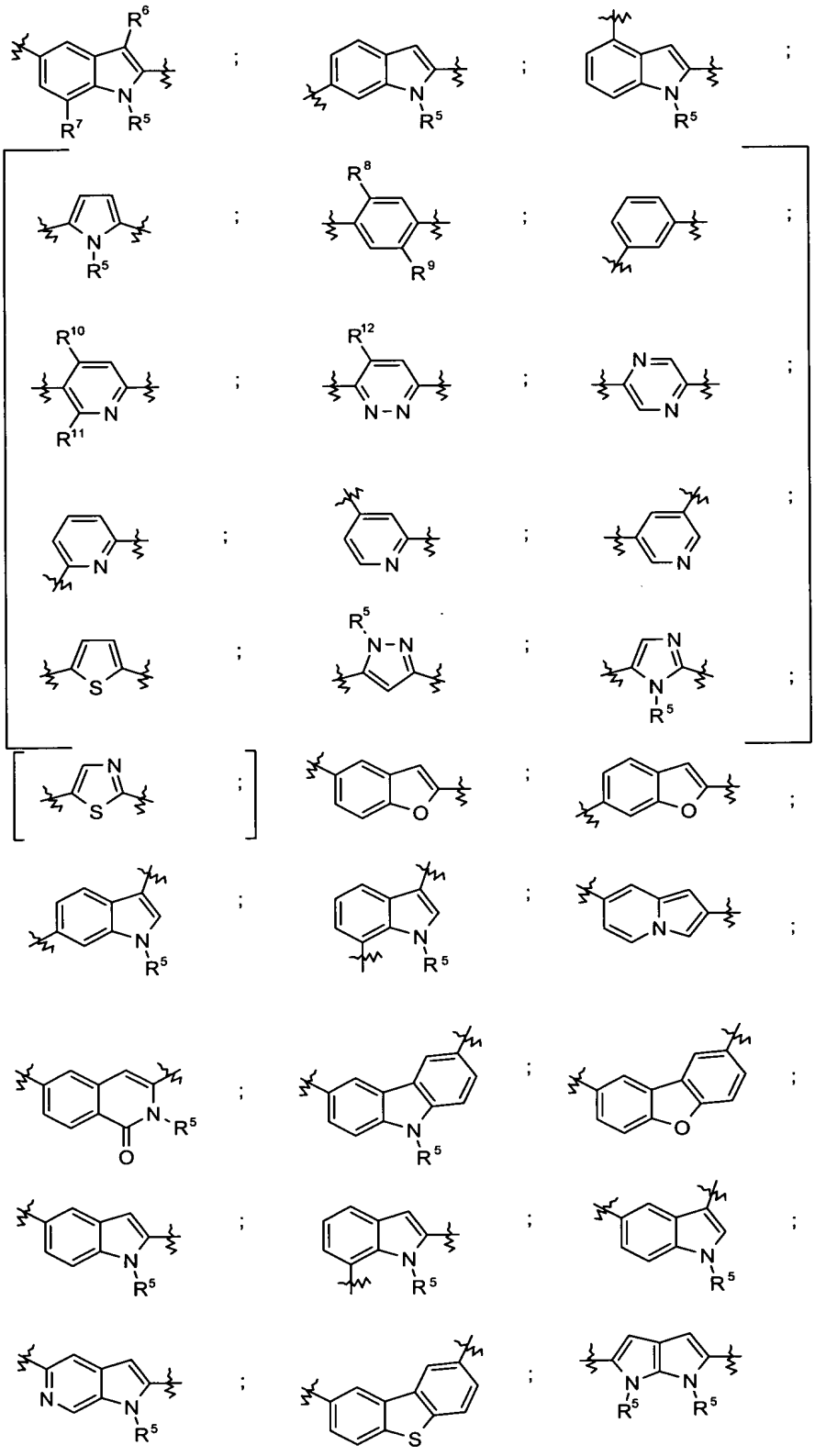
X^2 is **[aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkenyl, alkynyl, cycloalkyl or heterocyclic]** **a fused bicyclic or tricyclic heteroaryl group:**

X^1 and X^3 are independently aryl, substituted aryl, heteroaryl, substituted heteroaryl, or -CHR^4, wherein R^4 is natural or unnatural amino acid side chain;

or a pharmaceutically acceptable acid addition salt thereof.

3. (canceled)

5. (Amended) The compound of Claim **[3]**2, wherein X^2 is **[an aryl, substituted aryl, heteroaryl or substituted heteroaryl moiety]** selected from a group consisting of the following moieties:



wherein,

R^5 is hydrogen, alkyl or substituted alkyl;

R^6 is hydrogen, alkyl, halo or alkoxy; **and**

R^7 is hydrogen, alkyl or halo**[;**

R^8 is hydrogen, alkyl, substituted alkyl, alkoxy or halo;

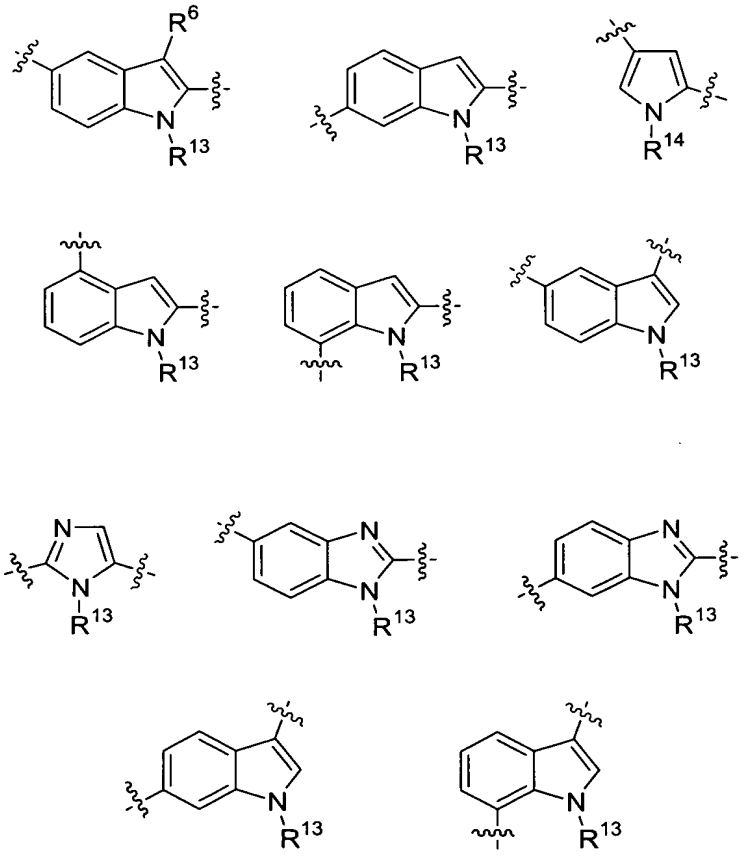
R^9 is hydrogen, alkyl, substituted alkyl, alkoxy, nitro or halo;

R^{10} is hydrogen or alkyl;

R^{11} is hydrogen or alkyl; and,

R^{12} is hydrogen or alkyl].

6. (Amended) The compound of Claim 2, wherein X^1 and X^3 are heteroaryl or substituted heteroaryl moieties independently selected from a group consisting of the following moieties:



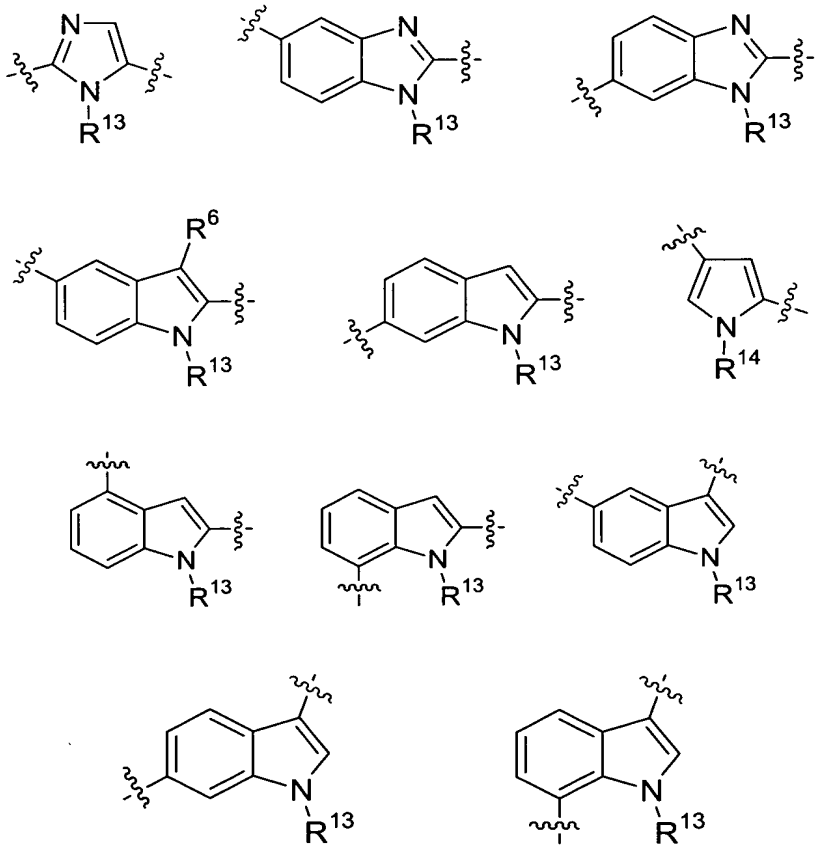
wherein

R^6 is hydrogen, alkyl, halo or alkoxy;

R^{13} is hydrogen **[of]**or alkyl; and,

R^{14} is hydrogen, alkyl or substituted alkyl.

9. (Amended) The compound of Claim 5, wherein X^1 and X^3 are heteroaryl or substituted heteroaryl moieties independently selected from a group consisting of the following moieties:

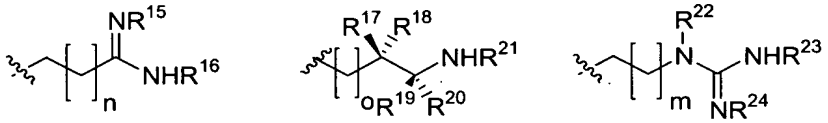


wherein

R^{13} is hydrogen **[of]** or alkyl;

R^{14} is hydrogen, alkyl or substituted alkyl;

and wherein R^1 and R^2 are substituted alkyl moieties independently selected from a group consisting of the following moieties:



wherein

R^{15} is hydrogen, hydroxyl, alkoxyl, alkyl, cycloalkyl or R^{15} and R^{16} together with the atoms to which they are attached form a heterocyclic ring;

R^{16} is hydrogen, hydroxyl, alkyl or cycloalkyl;

R^{17}, R^{18}, R^{19} and R^{20} are independently hydrogen or alkyl;

R^{21} is hydrogen alkyl, substituted alkyl, cycloalkyl or acyl;

R^{22} is hydrogen or alkyl, or R^{22} and R^{23} together with the atoms to which they are attached form a heterocyclic ring, or R^{22} and R^{24} together with the atoms to which they are attached form a heterocyclic ring.

R^{23} is hydrogen, hydroxyl, alkyl, cycloalkyl or R^{23} and R^{24} together with the atoms to which they are attached form a heterocyclic ring;

R^{24} is hydrogen, hydroxyl or alkyl;

m is 1, 2 or 3;

n is 1, 2 or 3; and,

o is 0, 1, 2 or 3.

18.(canceled)

24. (New) A pharmaceutical formulation comprising a pharmaceutically acceptable excipient and a anti-bacterially or anti-fungally effective amount of a compound of any one of claims 1, 2, or 4 - 17.